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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/018,964	04/11/2002	Bruce M. Paterson	11613.33USWO	6025

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NATIONAL INSTITUTES OF HEALTH
P. O. BOX 2903
MINNEAPOLIS, MN 55402

EXAMINER	
SWOPE, SHERIDAN	

ART UNIT	PAPER NUMBER
1656	

DATE MAILED: 10/18/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/018,964	PATERSON ET AL.	
	Examiner	Art Unit	
	Sheridan L. Swope	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 August 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 3-11* is/are pending in the application.

4a) Of the above claim(s) *6-9* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-5,10 and 11* is/are rejected.

7)☒ Claim(s) *1, 3-5, 10, and 11* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☑ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The Art Unit location of your application in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Art Unit 1656.

Applicant's response, on August 22, 2005, to the First Action on the Merits of this case, mailed April 21, 2005, is acknowledged. It is acknowledged that applicants have cancelled Claim 2, amended Claims 1, 3, and 5, and added Claims 10 and 11. Claims 1 and 3-11 are pending. Claims 6-9 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected inventions, there being no allowable generic or linking claim. Claims 1, 3-5, 10, and 11 are hereby considered.

Specification-Objections

Objection to the specification for not disclosing the structure of the myoD or the cyclin-dependent kinase 4 (CDK4) used in the Working Examples is maintained. In support of their request that said rejection be withdrawn, Applicants provide the following arguments. The specification provides, on pages 31 and 9, that clone CMD1 of chicken MyoD was used (pg 31, line 20), wherein said clone is described in GenBank Accession No. L34006 (Dechesne et al, 1994). The specification provides, on page 33, that the CDK4 used is as described in Kato et al, 1993.

These arguments are not found to be persuasive. It is acknowledged that the specification, at page 31, discloses the structure of the MyoD used in the analysis of protein/protein interaction in C2C12 cells, the Working Example of Section IX. It is also acknowledged that the specification, at page 33, discloses the structure of the CDK4 used for

mapping the region of MyoD that binds CDK4, the Working Example of Section XI. However, the specification fails to disclose the structure of the MyoD used in Working Examples I-VIII and X-XIII or the structure of CDK4 used in Working Examples I-X, XII, and XIII. Therefore, objection to the specification for not disclosing the specific sequence of the myoD or the CDK4 used in the Working Examples is maintained.

Claims-Objections

Objection to the Claims 1and 3-5, for failing to recite a sequence identifier number for the elected sequence, is maintained. New Claims 10 and 11 are objected to for the same reason. In support of their request that said rejection be withdrawn, Applicants provide the following argument. Claims 1 and 3 have been amended to refer to SEQ ID NO: 1 corresponding to the sequence Tyr-Ser-Gly-Pro-Pro-Xaa-Xaa-Xaa-Arg-Arg-Xaa-Asn-Xaa-Tyr-Xaa, which encompasses the elected sequence.

This argument is not found to be persuasive. The MPEP (2421.02) states:

> "Basically, the sequence rules define a set of symbols and procedures that are both mandatory and the only way that an applicant is permitted to describe information about a sequence that falls within the definitions used in the rules.
>
> The sequence rules embrace all unbranched nucleotide sequences with ten or more bases and all unbranched, non-D amino acid sequences with four or more amino acids, provided that there are at least 4 "specifically defined" nucleotides or amino acids. The rules apply to all sequences in a given application, whether claimed or not. All such sequences are relevant for the purposes of building a comprehensive database and properly assessing prior art. It is therefore essential that all sequences, whether only disclosed or also claimed, be included in the database."

The sequence listing should be corrected to disclose all sequences, of four or more residues, that are disclosed in the claims and/or specification.

Objection to Claims 1 and 3-5 for reciting non-elected subject matter is maintained, as the claims have not been amended to recite only the elected subject manner.

Claim Rejections - 35 USC § 112-Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Rejection of Claims 1 and 3-5 under 35 U.S.C. 112, second paragraph, as being indefinite for the reasons set forth in the prior action, is maintained. New Claims 10 and 11 are rejected for the same reasons. In support of their request that said rejection be withdrawn, Applicants provide the following argument. Applicants have amended claims 1, 3, and 5 to obviate this rejection. Specifically, the term "CDK-4" has been replaced with "cyclin-dependent kinase 4", which is well understood by those of skill in the art.

This argument is not found to be persuasive for the following reasons. As explained in the prior action, the specification fails to define the structure of the "cyclin-dependent kinase 4" (CDK4) proteins that bind any "CDK4 binding peptide". The specification, at page 1, lines 12-14, defines CDK4 as "a major catalytic subunit of mammalian D-type cyclins, which act during the G_1 phase of the cell cycle to enforce the decision of cells to enter the S phase". As previously explained, said definition for CDK4 includes an extremely large number of naturally-occurring known and unknown proteins as well as variants thereof; the specification fails to provide any structural limitations. Moreover, the functional limitations provided by said definition, do not differentiated CDK4 from other cyclin-dependent kinases. The specification states: "Three D-type cyclins (D1, D2 and D3) are differentially expressed in proliferating cells in response to various growth factor mediated signals. The D-type cyclins interact combinatorially with CDKs 2, 4, 5 and 6 to form active holoenzymes that facilitate progression through the G_1 phase of the cell cycle into S phase." In addition, it is known in the art that CDKs

can be functionally redundant in their ability to regulate the cell cycle (Morgan, 1997; page 264-265; Table 1). Since Claims 1, 3-5, 10, and 11 recite a polypeptide that binds to any one of an extremely large number of "cyclin-dependent kinase 4 proteins", a person of ordinary skill in the art of would not know the metes and bounds of the recited invention. For these reasons and those provided in the prior action, rejection of Claims 1 and 3-5 under 35 U.S.C. 112, second paragraph, as being indefinite, is maintained. New Claims 10 and 11 are rejected under 35 U.S.C. 112, second paragraph, for the same reasons.

Claim Rejections - 35 USC § 112-First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Enablement

Rejection of Claims 1 and 3-5 under 35 U.S.C. 112, first paragraph, for lack of enablement, for the reasons set forth in the prior action, is maintained. As described in the prior action, the specification does not reasonably provide enablement for any polypeptide comprising any peptide having the sequence Tyr-Ser-Gly-Pro-Pro-Xaa_1-Xaa_2-Xaa_3-Arg-Arg- Xaa_4-Asn-Xaa_5-Tyr- Xaa_6, wherein Xaa_1 is Cys or Ser, Xaa_2 is Ser or Gly, Xaa_3 is Ser, Ala, or Pro, Xaa_4 is Arg or Gln, Xaa_5 is Ser, Cys, or Gly, and Xaa_6 is Asp or Glu, wherein said polypeptide binds to any protein having any structure and having CDK4 activity. New Claims 10 and 11 are herein rejected for the same reasons.

In support of their request that said rejection be withdrawn, Applicants provide the following arguments. The region of myoD that mediates binding with CDK4 has been

determined. Those residues that are conserved, across species, for said region of myoD have been identified. The preservation of a consensus sequence implies functional importance (Alberts et al, 2002; attached). The claims have been amended to recite the functional limitation of binding to CDK4.

These arguments are not found to be persuasive for the following reasons. It is acknowledged that Applicants have identified the region of chicken myoD that binds to CDK4 as being the peptide YSGPPCSSRRRNSYDS (Example XI; Fig 14; Zhang et al, 1999-IDS). The specification also discloses an alignment between said peptide and similar peptides in myoD from other organisms, including the elected human peptide. Some of the amino acid residues found in the chicken peptide are also found in the peptides from other organisms. However, neither the specification nor the prior art provide any evidence that the human peptide, or any of said peptides from other organisms, can bind any CDK4 protein. Similarly, neither the specification nor the art provide evidence that any of said conserved amino acid residue are necessary for the recited binding. The Alberts et al, 2002 reference has not been provided to the Examiner and, if Applicants wish for said reference to be considered, it should be supplied. Nonetheless, as explained in the prior action, the results of modifying any protein are unpredictable (Wishart et al, 1995; Witkowski et al, 1999) and the unpredictability increases as the knowledge of the relationship between the protein's structure and its function goes down. Herein, only a single protein comprising only a single peptide having the desired activity has been disclosed; thus, very little is known about the structure/function relationship. In addition, an alignment of chicken myoD with myoD from the other organisms demonstrates that, the putative consensus sequence is not a region of high conservation, compared to the level of

conservation within other regions of the myoD proteins (see enclosed alignments). Moreover, Applicant's own art is inconsistent with, and appears to teach away from, the recited invention. Zhang et al, 1999 (IDS) teach that myoD homologs from *Drosophila* and *C. elegans* bind CDK4 and inhibit cell growth (pg 6988, parg 3). However, neither of said homologs comprises any one of the putative consensus sequences disclosed in Figure 14 herein. Applicants have disclosed only a single protein comprising only a single peptide that binds CDK4. Said disclosure is insufficient to enable a skilled artisan to make and use the full scope of the instant invention. Therefore, rejection of Claims 1 and 3-5 under 35 U.S.C. 112, first paragraph, for lack of enablement, for the reason described in the prior action and above, is maintained. New Claims 10 and 11 are rejected for the same reasons.

Written Description

Rejection of Claims 1 and 3-5 under 35 U.S.C. 112, first paragraph, for insufficient written description, for the reasons described in the prior action, is maintained. New Claims 10 and 11 are rejected under 35 U.S.C. 112, first paragraph, for the same reasons. In support of their request that said rejection be withdrawn, Applicants provide the following arguments. Figure 14 shows five different species of the 15-residue sequence along with a consensus sequence. Therefore, Applicants have disclosed five different species within the claimed genus and the invention is adequetly described. Claims 1 and 3 now recite a peptide that binds "cyclin-dependent kinase 4", a protein known in the art.

These arguments are not found to be persuasive for the following reasons. It is acknowledged that Figure 14 shows five peptides and the regions of homology between them. However, the specification describes only one protein comprising only one of said peptides,

wherein the protein binds any CDK4. The specification fails to describe any other protein, comprising any of the recited peptides, wherein the protein binds any CDK4. In addition, since the phrase "cyclin-dependent kinase 4" renders Claims 1, 3-5, 10, and 11 indefinite, the added functional limitation of binding to "cyclin-dependent kinase 4" fails to adequately describe the invention. For these reasons and those presented in the prior action, rejection of Claims 1 and 3-5 under 35 U.S.C. 112, first paragraph, for insufficient written description, is maintained. New Claims 10 and 11 are rejected under 35 U.S.C. 112, first paragraph, for insufficient written description, for the same reasons.

Applicant's amendment necessitated any new grounds of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sheridan L. Swope whose telephone number is 571-272-0943. The examiner can normally be reached on M-F; 9:30-7 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr can be reached on 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published application may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on the access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Sheridan Lee Swope, Ph.D.

Art Unit 1656

SHERIDAN SWOPE, Ph.D.
PATENT EXAMINER